

The Waldmann article describes the use of *unlabelled* anti-Tac in patients with ATL. These patients are described to have a “pretherapy serum soluble IL-2R (sIL-2R $\alpha$ ) levels of 920 to 230,370 U/mL”. (see page 1703, col. 2, lines 7-8 of “Results” section). The “initial basic protocol” as described in column 2 on page 1704, states that the anti-Tac therapy “involved the administration of 20 mg anti-Tac on two occasions during the first week and 40 mg anti-Tac on two occasions during the second week of therapy for each patient (Table 2)”. Based upon the results of these initial treatment protocols the dosages were altered, which is described on page 1705, column 2. Here, Waldmann states:

In light of these early observations, to achieve a rapid saturation of IL-2R, the basic dosing schedule was altered for the final 10 patients in the group so that 50 mg anti-Tac per patient was administered on two occasions during the first week of therapy and on two occasions during the second week of therapy.

Thus, the Waldmann article teaches that it is preferred to use a 50 mg anti-Tac dose, in order to saturate IL-2R.

Several important features of this study distinguish it from the claimed invention. First, although the patients had a broad range of soluble IL-2R levels (see Waldmann (Blood) Table 1) ranging from 920 to 230,370 U/mL, all of the patients were given the same amount of anti-Tac. In contrast, the claimed invention provides different dosages for patients having sIL-2R levels of less than 2000 U/mL, sIL-2R levels of 2000 to 10000 U/mL, sIL-2R levels of 10,000 to 50,000 and sIL-2R levels greater than 50,000 U/mL. No such distinction is described in the Waldmann article. Second, the Waldmann article describes administering dosages of 20 to 50 mg anti-Tac per dose, preferably 50 mg. The claimed invention utilizes a lower dosage range, wherein patients having sIL-2R levels of less than 2,000 units/ml receive a dose of 2 mg anti-

Tac, patients having sIL-2R levels of 2,000 - 10,000 units/ml receive a dose of 5 mg of anti-Tac, patients having sIL-2R levels of 10,000 - 50,000 units/ml receive a dose of 10 mg of anti-Tac and patients having sIL-2R levels of greater than 50,000 units/ml receive a dose of 20 mg of anti-Tac. Finally, the Waldmann article describes a study using unlabelled anti-Tac, whereas the present invention claims the use of yttrium-conjugated anti-Tac.

Based upon these distinguishing features, applicant asserts that the Waldmann (Blood) article does not anticipate or make obvious the claimed invention. As the Examiner well knows, an anticipatory reference must teach each and every element of the claim. Obviousness requires that the differences between the claimed subject matter and the prior art are such that "the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. §103; *Custom Accessories, Inc. v. Jeffrey-Allan Indus., Inc.*, 807 F.2d 955, 958 (Fed. Cir. 1986). Waldmann does not teach or suggest the use of varying sIL-2R levels to determine the dosage of anti-Tac. The skilled artisan could not determine the correct dose of <sup>90</sup>Y-conjugated anti-Tac based upon the Waldmann article. Also, the Waldmann reference does not teach or suggest the use of low doses of anti-Tac; i.e. less than 20 mg per dose. Furthermore, the Waldmann reference does not teach or suggest a <sup>90</sup>Y-conjugated anti-Tac can be used at the claimed dosage ranges having the claimed levels of radioactivity. Based upon these missing elements of claim 27, the claim is not anticipated by Waldmann. Furthermore, these missing elements could not be determined by one skilled in the art based upon the Waldmann (Blood) article. In fact, the skilled artisan reading the Waldmann article would conclude that there is no correlation between sIL-2R levels and anti-Tac dosage, let alone <sup>90</sup>Y-conjugated anti-Tac. Thus, the subject matter of claim 27 as a whole was not made

obvious by the Waldmann article to the skilled artisan at the time of the invention. Applicant respectfully requests reconsideration and withdrawal of the §102(b)/§103 rejection.

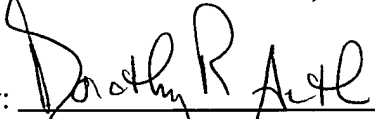
No additional fee is believed to be necessary.

The Commissioner is hereby authorized to charge any additional fees which may be required for this response, or credit any overpayment to Deposit Account No. 13-4500, Order No. 2026-4003US3.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition and for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. 13-4500, Order No. 2026-4003US3. A DUPLICATE COPY OF THIS SHEET IS ATTACHED.

Respectfully submitted,

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